West Virginia Expert Pain Management Panel

Safe & Effective Management of Pain Guidelines

2016

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Executive Summary

Prescription medications are an integral part of improving the quality of life for millions of Americans living their lives with acute or chronic pain. However, one of the most serious public health problems in our country is the over dependence on these substances, with particular attention to the opioid class of prescription pain medications. Opioid addiction also accounts for a vast amount of indirect causes of crime such as theft, injury, and murder stemming from the need to acquire these substances whether legally, via prescription, or illegally, on the streets.

Americans, constituting only 4.6% of the world's population, have been consuming 80% of the global opioid supply, and 99% of the global hydrocodone supply, as well as two-thirds of the world's illegal drugs (Pain Physician, 2010). Approximately 2 million Americans live with prescription opioid abuse or dependence (SAMSHA, 2013). About 75% of opioid addiction disease patients switch to heroin as a cheaper opioid source (SAMSHA, 2013). During 2014, 47,055 drug overdose deaths occurred in the United States (MMWR, January 1, 2016). In 2014, 61% (28,647) of drug overdose deaths involved some type of opioid, including heroin (MMWR, January 1, 2016). Therefore, approximately 78 Americans die every day due to prescription drug overdose, equating to one American dying approximately every 20 minutes. Additionally, in our country a baby is born addicted to opioids approximately every 25 minutes (Tolia, 2015). In the 1990's, pain was introduced as the "fifth vital sign" which was accompanied by pharmaceutical company efforts to market directly to prescribers (Lanser P, 2001). Furthermore, studies have shown a strong and consistent linear relationship between the amount of opioids sold and distributed with morbidity and mortality associated with these chemicals (Paulozzi LJ B. D., 2006). These staggering statistics demonstrate how bad this situation is, and why it has been generally regarded as a national epidemic (Paulozzi LJ J. C., 2011) (Jones CM, 2013).

As with any epidemic, the usual course of action to rid the population of it includes prevention, treatment, and elimination of the source of the problem. Prevention of opioid overdose includes strategies such as education on appropriate pain management with or without opioid prescription medications, and increasing the awareness and availability of naloxone as the antidote for respiratory failure, and eventual death, from inappropriate opioid use. Treatment of this national epidemic includes providing the appropriate therapy for those experiencing substance use disorder (as per DSM-V, formerly known as addiction) whether through psychological therapy and/or medication assisted therapy (MAT). Elimination of the substance for this national epidemic involves reducing the supply from the population with strategies such as proper opioid medication storage and disposal.

West Virginia (WV) has the highest national state-by-state drug overdose death rate of 35.5 per 100,000 (Age Adjusted), with a large margin over the next closest state of New Mexico having a rate of 27.3, while the national average is 14.7 (MMWR, January 1, 2016). WV is one of twenty-nine states receiving funding from the Centers for Disease Control (CDC) Prescription Drug Overdose: Prevention for States Program aiming to maximize Prescription Drug Monitoring Programs (PDMPs), provide community or Insurer/Health System Interventions, and conduct policy evaluations (CDC Prevention for States, 2016). This program has aided in the formation of a geographically and professionally diverse expert panel of West Virginia professionals with intentions of building upon the CDC Chronic Pain Opioid Guidelines of 2016 to:

- Develop clinical pain management guidelines based on best practices, clinical experience, and evidence-based literature.
- Develop a risk reduction strategy for the appropriate use of opioid prescription pain medications to improve health outcomes.

This overall pain management guidance is intended for both prescribers and dispensers as an expansion to the 2016 CDC Chronic Pain Opioid Guidelines (CDC, 2016). In addition to the clinical applications of this overall pain management guidance, there is also an educational value from incorporating the safe and effective management of pain as a mandatory and significant component of all healthcare professional school curriculum. Furthermore, the education can be incorporated into continuing educational programs for current healthcare professionals. Adapting to updated chronic medical condition treatment guidelines, whether pain, diabetes, or hypertension, is critical to the advancement of patient care. The collaboration and education of legislators, law enforcement, the healthcare community, and the public will provide the ability to stop living in the problem and begin to live in the solution.

The following guidance is a summary of the work and efforts put forth by this expert pain management panel, with hopes of not only improving human quality of life, but also to save lives by promoting the values of safely and effectively managing pain for those suffering.

Expert Pain Management Panel Members

Panel Member	Organization/Title
Mark Garofoli, PharmD, MBA (Coordinator)	West Virginia University (WVU) School of Pharmacy, Assistant Professor
Timothy Deer, MD (Chairperson)	Centers for Pain Relief President/CEO, & INS President
Richard Vaglienti, MD (Vice Chairperson)	WVU Pain Management Specialist
Rahul Gupta, MD	West Virginia DHHR, Public Health Commissioner & State Health Officer
Ahmet Ozturk, MD	Marshall University & Huntington Pain Specialist
Denzil Hawkinberry, MD	Community Care of West Virginia Pain Specialist
Bradley Hall, MD	WV Medical Professionals Health Program Executive Medical Director
Matt Cupp, MD	Board Certified Pain Management Specialist
Michael Mills, DO	West Virginia Office of Emergency Medical Services Director
Jimmy Adams, DO	Active Physical Medicine & Pain Center
Richard Gross, PhD	WVU Pain Management Psychologist
Jason Roush, DDS	West Virginia State Dental Director
Stacey Wyatt, RN	St. Francis Hospital Pain Specialist
Vicki Cunningham, RPh	WV Bureau of Medical Services, Pharmacy Services Director
Felice Joseph, RPh	PEIA Pharmacy Director
Stephen Small, RPh, MS	Rational Drug Therapy Program Director
Patty Johnston, RPh	Colony Drug & Wellness Center, Former Owner (Beckley)
Charles Ponte, PharmD, CPE	WVU Schools of Pharmacy & Medicine
James Jeffries, MS	WV DHHR, Division of Infant, Child, & Adolescent Health, Director
Michael Goff	West Virginia Prescription Drug Monitoring Program, Administrator

Risk Reduction Strategy

A major concern of healthcare professionals and patients alike is the question of what is the "gold standard" approach to managing pain especially chronic pain. Pain management strategies have been largely based upon subjective evaluation methods versus more objective assessments. Treatments derived from a more objective approach (i.e. hypertension and hyperlipidemia) will be viewed more positively by all constituencies. This overall pain management guidance, included herein, and in no particular order, provides healthcare professionals with a risk reduction process which will improve patient care and minimize provider anxiety.

1. Risk Screenings

All patients being considered for chronic opioid therapy should be screened for risk of substance misuse. Screen for this risk before prescribing opioids. Importantly, patients who have been taking opioids for long periods of time should also be routinely screened. There are a number of screening tools with good predictive value that have been developed specifically to screen for risk of opioid misuse in the context of chronic pain treatment. Although more in-depth research on evidence may be needed (Chou R e. a., 2009), these tools may be useful in determining relative risk in addition to the medical history. ("Opioid Risk Assessment Tools", 2016)

a) Patients Being Considered for Opioid Therapy
   i. Opioid Risk Tool, ORT (Appendix 1.1)
   ii. Drug Abuse Screening Test, DAST (Appendix 1.2)
   iii. Diagnosis, Intractability, Risk, & Efficacy Score, DIRE (Appendix 1.3)
b) Patients Already Receiving Opioid Therapy
   i. Current Opioid Misuse Measure, COMM (Appendix 1.4)
   ii. Pain Medication Questionnaire, PMQ (Appendix 1.5)
   iii. Prescription Drug Use Questionnaire, PDUQ (Appendix 1.6)

The use of a risk screening tool has the ultimate purpose of assisting in the selection of the safest treatment options for any individual patient. The higher the risk of abuse for any individual patient corresponds with less appropriateness for the use of controlled substances because of their habit-forming or abuse tendencies, and an increased need for counseling and monitoring the respective patient for the given risk factors.

2. Drug Interaction & Pharmacogenics Review

Pharmacogenics (PGx) is the study of the role of genetics in drug response. In general, there can be genetic variability in multiple physiological systems of the human body (i.e. hepatic enzymes, drug receptors, drug transport genes, etc.) resulting in altered drug-responses. Three of the most common hepatic cytochrome P450 (CYP450) enzymes that have shown distinct differences in genetic variability are 2C9, 2C19, and 2D6. 2C9 substrates include pain medications such as ibuprofen, and celecoxib, while 2C19 substrates include diazepam, and 2D6 substrates include codeine, dextromethorphan, tramadol, duloxetine, venlafaxine, and tricyclic antidepressants. A chart illustrating the PGx metabolic differences within the population is available in Appendix 2.0 (Singh, 2008).

When available and appropriate to the treatment regimen, this testing can be very helpful in ensuring an appropriate response to a medication such as codeine or tramadol. A CYP2D6 poor metabolizer may not receive adequate analgesia from codeine or tramadol, whereas, an ultra-rapid metabolizer may experience unnecessary side effects (or even overdose) because of having more of the active metabolites present. This scenario emphasizes the need to not only review a patient's medication regimen for drug-drug interactions (such as those on page 81 of this document) as a standard of care, but also drug-gene interactions.

To best treat patients in pain with these types of medications, common pharmacogenetic tests can be performed on blood, saliva, or cheek swabs by multiple testing companies. Patients should be reminded of the special privacy protections for their personal genetic information under the Genetic Information & Nondiscrimination Act (GINA) of 2008 (Commission, 2008). Testing typically costs a few hundred dollars and may be covered by third-party payers. Pharmacogenetic medication dosage guidelines are available via the PharmGKB website at: www.pharmgkb.org

3. Patient & Provider(s) Agreements

In order to encourage and emphasize the importance for proper use of any pain medications, it is important to make sure that both a patient and provider(s) have reviewed the realistic expectations of therapy (pain reduction and improved functional status). Establishing a "Patient and Provider Agreement" (previously referred to as a patient contract, consent, or agreement) is an invaluable tool to ensure a mutual commitment from the patient and the provider(s) to achieve and maintain treatment goals, while also stating any reasons for agreement termination.

Items to include in a Patient & Provider(s) Agreement (Appendix 3.0)

Patient & Provider(s) Agreement Examples

a) American Association for Pain Management, AAPM (Appendix 3.1)
b) Pain.Edu, typical (Appendix 3.2)
c) Pain.Edu, low-literacy (Appendix 3.3)
d) Veterans Affairs, VA (Appendix 3.4)

4. Pain Reduction and Function Improvement Goal

Pain should be thoroughly evaluated before prescribing medications or other treatments. The successful treatment of chronic pain involves a long-term process of monitoring and adjusting treatment as necessary. A patient's functional status, including activities of daily living, is often severely affected by pain. Inadequate treatment can considerably affect a patient's quality of life, or cause them to display drug-seeking behaviors when they are in fact only seeking relief from chronic pain. ("Opioid Risk Assessment Tools", 2016)

In addition to pain severity, pain can be evaluated based on how it affects a patient's functional status and performance of daily activities. The goal is to reduce pain and improve a patient's daily social and physical function. However, there are some clinical circumstances under which reductions in pain without improvement in physical function might be a more realistic goal (i.e. diseases typically associated with progressive functional impairment or catastrophic injuries such as spinal cord trauma (CDC, 2016).

Many common numeric scales merely ask subjective questions on how a patient personally views his or her pain with no relative markers for comparison to general pain conditions. Three pain function scales including The PEG Pain Screening Tool (Appendix 4.1), The Graded Chronic Pain Scale (Appendix 4.2), & The Brief Pain Inventory Short Version (Appendix 4.3) assess beyond these parameters and are provided in Appendix 4.0. The first two of these scales are within the Updated 2015 Washington State Opioid Guidelines (Group, May 2015) and the "PEG" Scale more directly comes from its original evaluation in 2009 (Krebs EE, 2009).

5. End of Therapy Goal

Any S.M.A.R.T. Goals (Specific, Measurable, Attainable, Realistic, and Timely) have a foundation around being able to be measurable in accordance with time. Thus, in setting appropriate pain management goals with patients, a timely plan of action in regards to achieving and maintaining a reduction in pain is required. With the acute management of pain, it is recommended to develop an end of therapy goal for any pain management medications based on the expected time frame of the healing process. Pain may become chronic in some cases, however for the management of acute pain syndromes (i.e. fractures, etc.) there should be an end of therapy goal for pharmacological management in order to prevent any unnecessary long term issues (i.e. adverse effects, dependency, etc.). In chronic pain management, these goals may be more difficult since the resolution of the syndrome, or the elimination of pain, is not expected to occur.

6. Psychological Evaluation

Initial and annual psychological evaluation should be considered for selected patients taking opioid pain medications. Risk is not a static variable yet it changes as life circumstances change and the psychological evaluation allows for assessment of these modifiable risk factors. For example, we know depression is a significant risk factor for worsening chronic pain as is stress- both of which can change with alteration in life circumstances. When appropriate, re-evaluation using appropriate tools allows for objective quantification of benefits with opioids, i.e. improvement in perceived disability, pain related worry, mood, and pain reduction. In some settings the primary care provider has expertise in the treatment and counseling of psychological comorbidities. If the primary care provider is also treating these conditions, careful documentation should be noted when evaluation is performed.

Currently the PHQ-2 depression screening instrument (Appendix 5.1) is a major suggested screening tool for depression, which is followed up with the PHQ-9 depression screen (Appendix 5.2). The purpose of the PHQ-2 is not to establish a final diagnosis or to monitor depression severity, but rather to screen for depression as a "first step" approach. Patients who screen positive should be further evaluated with the PHQ-9 to determine whether they meet criteria for a depressive disorder. Another useful depression screening is the Beck's Depression Inventory, which is provided in Appendix 5.3.

7. Proper Medication Storage & Disposal

Healthcare professionals play a major role in educating patients, and that education is very important for the topic of proper medication storage and disposal. It's important to educate patients to keep medications in a secure storage location out of the reach and sight of children and pets, and to put medicines away after every use. Even simple measures like making sure that the safety cap is locked can help prevent accidents. (Education, 2016) Patients need to be educated that if an accidental ingestion does occur, one should contact the Poison Center (1-800-222-1-222) immediately or dial 911 if person is unconscious or having a seizure. Patients also need to be reminded to store medications in an area that is cool and dry since heat and humidity can damage medicines, hence why a bathroom is not a suitable location to store medications unless the room is well ventilated. However, the bathroom medicine chest is an ideal place to keep items such as bandages, tweezers, gauze, cotton balls, scissors, and other products that aren't affected by heat or humidity. Patients should be reminded that if there are children around or those with a history of substance abuse, or if storing any controlled substances, one should secure his/her medications within a lockable area such as in a safe, cabinet, or a drawer. (Administration, 2015) Patients also should be reminded to only take the number of doses needed when going outside the home or traveling. Overall, there is a need for emphasis of inaccessibility for anyone besides the intended patient.

The FDA recommends that most prescription medications be returned through a DEA sponsored Take-Back Program, a DEA-Authorized collector (https://www.deadiversion.usdoj.gov/pubdispsearch) or throwing away in household trash by removing medications from original container and mixing with an undesirable substance (i.e. coffee grounds, dirt, etc.) in a sealable container or bag. For a small number of medications, the FDA recommends immediate removal from the home by flushing them down the toilet or sink (Appendix 6.0). To dispose of a drug patch, carefully remove it by the edges and avoid touching the used medicine pad; then fold the patch in half, sticky sides together. (Education, 2016)

8. Naloxone Prescribing & Administration

Naloxone is the antidote or reversal agent for opioid overdose. Naloxone reverses the respiratory depression associated with opioid overdose. Naloxone is not a controlled substance, but requires a prescription from any healthcare professional with prescriptive authority or dispensing by a pharmacist (in states allowing such dispensing, such as WV). Naloxone is available in multiple formulations including a 0.4mg/ml IM injection, 0.4mg/ml auto-injection, 2mg/2ml intranasal solution, and the 4mg nasal spray.

Patient/family/friend candidates for being prescribed take-home naloxone (Appendix 7.1)

SAMHSA Naloxone Administration Guidelines (Appendix 7.2)

In March of 2016, at the request of the governor, the 2016 legislature passed Senate Bill 431, available online at www.legis.state.wv.us, authorizing licensed pharmacists or pharmacy interns (working under the guidance of licensed pharmacists) to dispense an opioid antagonist without a

prescription. A pharmacist or pharmacy intern who dispenses an opioid antagonist without a prescription shall report the dispensing in the PDMP and provide patient counseling (mandatory which the patient may not opt out) to the individual for whom the opioid antagonist is dispensed regarding, but not limited to:

- Proper administration;
- Importance of contacting emergency services (i.e. calling 911) as soon as practicable either before or after administering the opioid antagonist;
- Risks associated with failure to contact emergency services following administration of an opioid antagonist;
- Providing educational materials on opioid-related overdose prevention and treatment, and opioid antagonist administration (materials developed by the WV Board of Pharmacy).

For more information: http://stopoverdose.org/index.htm

For substance use disorder (addiction) and especially if one was in a scenario where naloxone was administered (whether personally, family, or friend), sources of help and education include:

- 1-844-HELP-4-WV (1-844-495-7498)
- SAMHSA Helpline: 1-800-662-4357 (1-800-662-HELP)
- Veteran's Crisis Line: 1-800-273-8255, Option 1
- Narcotics Anonymous (Personal): 818-700-0700
- Nar-Anon (Family/Friends): 1-800-477-6291
- WV Medical Professionals Health Program (Health Professionals): 304-933-1030

9. Prescription Drug Monitoring Program (PDMP) Use

Prescription drug monitoring programs (PDMPs), also known as Controlled Substance Monitoring Programs (CSMPs), must be fully utilized to reach their potential in controlling prescription drug abuse and diversion. However, in the majority of the 49 states with operational PDMPs, participation by prescribers and dispensers is voluntary, with utilization rates well below 50%. Recent experience in Kentucky, Tennessee, New York and Ohio indicates that mandating provider use of PDMPs can result in a rapid increase in enrollment and requests for prescription information (Brandeis University, October 2014).

Based on data from national surveys and information, these are the best practices for any state in utilizing a PDMP (Center, 2016):

- Adopt uniform and latest ASAP reporting standard;
- Collect positive identification for the person picking up prescriptions;
- Collect data on method of payment, including cash transactions;
- Reduce data collection interval; move toward real-time data collection;
- Integrate PDMP reports with health information exchanges, electronic health records, and pharmacy dispensing systems;
- Send unsolicited reports and alerts to appropriate users;
- Mandate enrollment & utilization;
- Delegate Access for internal staff/team;
- Enact and implement interstate data sharing among PDMPs;
- Secure funding independent of economic downturns, conflicts of interest, public policy changes, and changes in PDMP policies.

West Virginia regulations revolving around the mandatory use of the PDMP are provided in Appendix 8.0, and are available online at www.legis.state.wv.us as Senate Bill 437 of the year 2012. In summary, all licensees who dispense Schedule II, III, and IV controlled substances to residents of WV must provide the dispensing information to the WV Board of Pharmacy (BOP) at least every 24 hours. All licensed prescribers must check the PDMP at the initiation of opioid therapy and at a minimum of every year thereafter. A physician working in a pain management clinic must check the PDMP at the initiation of the controlled substance therapy and at a minimum of every 90 days thereafter. The West Virginia Controlled Substance Monitoring Program (CSMP) is available at:

https://www.csapp.wv.gov/Account/Login.aspx

10. Urine Drug Screening/Testing

Urine drug screening/testing is important in the monitoring of compliance of prescribed medications and detecting the use of illicit substances. All healthcare professionals need the most up-to-date and comprehensive medication information (i.e. prescription medications, over-the-counter medications, herbals, supplements, illicit substances, etc.) for a patient to improve the patient's longevity and quality of life. The timing of the urine drug screening/testing needs to be in line with the results being available before or at the point of treatment decisions.

Alternative Drug Screening Methods (Appendix 9.1)

Urine Drug Screening vs. Testing (Appendix 9.2)

Frequency of Screening/Testing (Appendix 9.3)

Urine Toxicology Detection Periods (Appendix 9.4)

Urine Drug Cross-reactants (Appendix 9.5)

Urine Drug Results (Appendix 9.6)

Consequences of Unintended Urine Drug Screening/Testing Results
If there are unintended urine drug screening/testing results, a careful re-assessment of the treatment plan must be completed. A patient's failure to adhere to the patient and provider agreement is not necessarily proof of abuse or diversion because it may be a result of inadequate pain relief, confusion regarding the prescription(s), a language barrier, or economic concerns. If uncertainty exists in regard to the nature of the unintended result, the provider(s) may consider arranging for an in-person meeting in order to have a non-judgmental conversation to clarify the patient's actions and concerns. If abuse or diversion is confirmed, treatment can continue with alternative therapies and consultation with a substance use disorder (addiction) specialist or psychiatrist and/or referral to a substance use disorder treatment program and/or law enforcement (if concern for the safety of others exists) should be considered.

11. Pill Counts

Randomized and/or Scheduled Pill Counts (based on appointments, etc.) are one way of attempting to improve proper medication adherence and prevent and/or detect medication diversion. Any patient who refuses to provide their medication for a random or scheduled pill count can be considered for discontinuation of that particular or any controlled substance or non-scheduled medication(s) while continuing treatment with alternative therapies. It is recommended to schedule any appointment-based pill counts (and the appointment itself) within a minimum of 3 to 5 days of when the current prescription will run out of supply/refills (Safeguard, 2011).

Process [One staff person will be assigned to: (Safeguard, 2011)]

1. Bring the patient to a private area of the clinic
2. Ensure that a staff person is present to witness this procedure
3. Request that the patient submit their medication to be counted and/or examined
4. Receive the medication from the patient
5. Count the medication on a clean flat object using sterile gloves or equipment.
6. Examine the color, shape and imprint of the tablet to insure the medication is the same as prescribed. a. If the medication is a capsule, the staff person shall examine the content of at least two capsules to ensure that the content has not been substituted. b. If the color, shape or imprint is questionable or the staff does not recognize the medication, the staff person shall query the color, shape and imprint of the tablet or capsule through a reputable pill identification resource.
7. Document the requested pill count, outcome and witness' name in the patient's record.
8. Advise the provider(s) of the outcome of the pill count.

Special Scenarios

Providers who are advised by their patient that the patient's medication was lost, destroyed, or stolen shall (Safeguard, 2011):

- Instruct patient to better secure their medication in the future.
- (If lost in fire) Retain a copy of any fire report (reflecting that a fire occurred) to be placed in the patient's medical record.
- (If stolen) Retain a copy of any law enforcement report (reflecting the theft) to be placed in the patient's medical record.
- Replacement of lost or stolen medication is at the discretion of the provider and/or based upon the patient & provider(s) agreement.

12. Drug Enforcement Agency (DEA) Red Flags

Healthcare professionals have an ethical and legal obligation to both prevent prescription drugs from being diverted to nonmedical uses, and to ensure patients receive safe and effective care involving healthcare professionals practicing in the usual course of their professional practice and treating a patient's legitimate medical condition. The US DEA has provided the following "red flags" as a resource of what to watch for as healthcare professionals to ensure that appropriate care is in place.

Prescriber

1. Cash only patients and/or no acceptance of worker's compensation or private insurance
2. Prescribing of the same combination of highly-abused drugs
3. Prescribing the same, typically high, quantities of pain drugs to most or every patient
4. High number of prescriptions issued per day
5. Out-of-area patient population

Dispenser

1. Dispensing a high percentage controlled to non-controlled drugs
2. Dispensing high volumes of controlled substances generally
3. Dispensing the same drugs & quantities prescribed by the same prescriber
4. Dispensing to out-of-area or out-of-state patients
5. Dispensing to multiple patients with the same last name or address
6. Sequential prescription #s for highly diverted drugs from the same prescriber
7. Dispensing for patients of controlled substances from multiple practitioners
8. Dispensing for patients seeking early prescription fills

Clinical Treatment of Pain

Descriptions & Examples of Types of Pain

Nociceptive Pain

General Description:

- Pain arising from noxious stimuli affecting thermal, mechanical, or chemical receptors (nociceptors) in normal tissues.

General Examples:

- Arthritis, mechanical lower back pain, post-operative pain, sports/exercise injury, etc.

Somatic Nociceptive Pain

- Description: Outer organs, body walls, & limbs (bone/joints/muscle/skin) producing aching or throbbing, and is well localized.
- Examples: Ankle sprain, incisional pain, etc.

Visceral Nociceptive Pain

- Description: Internal organs; all thoraco-abdominal organs
- Examples: Localized tumor or hollow viscus, IBS, myocardial infarction, etc.

Neuropathic Pain

General Description

- Abnormal processing of sensory input by the Central Nervous System (CNS) and/or Peripheral Nervous System (PNS)

General Examples:

- Neuropathic Lower back pain, etc.

Central Neuropathic Pain

- Deafferentation
  - Injury to either the CNS or the PNS
  - Phantom pain (PNS) & burning pain below spinal cord injury/lesion (CNS)
- Sympathetic
  - Dysregulation of the autonomic nervous system
  - Complex Regional Pain Syndromes (CRPS)

Peripheral Neuropathic Pain

- Polyneuropathies
  - Pain is felt along the distribution of many peripheral nerves
  - Diabetic neuropathy, post-herpetic neuralgia, Guillain-Barre Syndrome pains, or alcohol-nutritional neuropathy
- Mononeuropathies
  - Usually associated with a known peripheral nerve injury, and pain is felt at least partly along the damaged nerve
  - Nerve root compression, nerve entrapment, trigeminal neuralgia

Mixed Pain

General Description:

- Combination of nociceptive and neuropathic pains

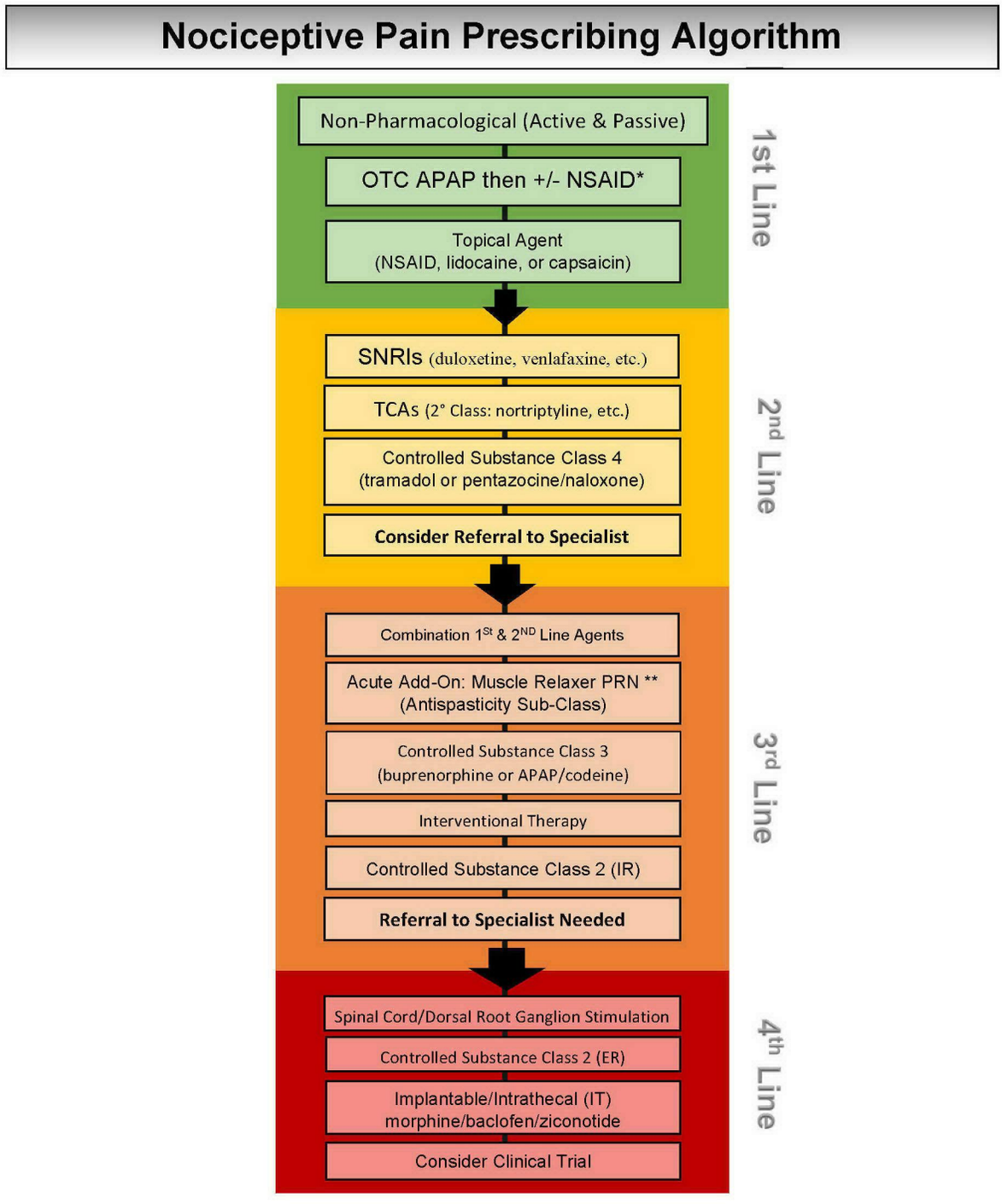
General Examples:

- Fibromyalgia, headache, lower back pain, myofascial pain syndrome, or skeletal muscle pain, etc.

Pain Treatment Algorithms

The intent of these clinical pain management treatment algorithms is to provide the best course of action for progression through escalating levels of pain management. These algorithms are meant to be referred to along with the 2016 CDC Chronic Pain Opioid Guidelines (CDC, 2016). Not every single entity must be attempted to progress to the next level, as every patient is unique, however, attempts to reduce a patient's pain and improve their daily function should follow the recommended treatment algorithm as closely as possible in order to provide the safest and most effective pain management for every patient. For instance, not every non-pharmacological treatment option must be attempted before progressing forward within each clinical treatment algorithm, however, a reasonable attempt should be made to try as many of the earliest treatment algorithm options as possible before progressing further. Whether considering or absolutely referring to a pain management specialist, the American Board of Anesthesiology (ABA), American Board of Pain Medicine (ABPM), or the American Board of Interventional Pain Physicians (ABIPP) have established and distinguishing certifications.

Pain Treatment Algorithms



ATTENTION:

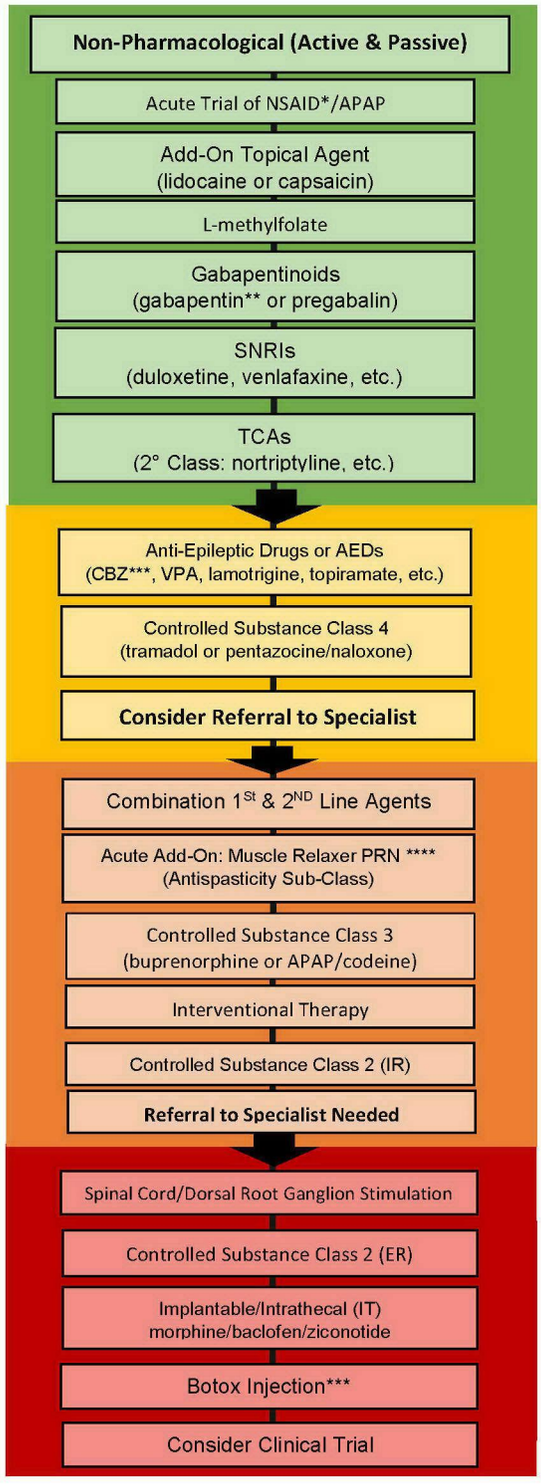
- Start at lowest dose and slowly taper up to maximum dose of one agent before adding or starting another drug.
- Depending on patient specifics, can maneuver within Line/Color Zones
- Intrathecal opioids are more effective than oral in patients unsuccessful on oral opioids.
- *Based on GI/Cardio Patient History
- **Watch for concominant CNS Depression

ABBREVIATIONS:

OTC: Over-the-Counter
APAP: Acetaminophen
NSAID: Non-Steroidal Anti Inflammatory Drug
ASA: Aspirin
IBU: Ibuprofen
SNRI: Serotonin Norepinephrine Reuptake Inhibitor
TCA: Tryclic Antidepressant
IR: Immediate Release
PRN: As Needed

1. Hooten WM, Timming R, Belgrade M, et al. Assessment and Management of Chronic Pain. [updated November 2013]. Institute for Clinical Systems Improvement. Available at https://www.icsi.org/_asset/bw798b/ChronicPain.pdf. Accessed July 6, 2015.
2. Christian J, Darnall B, Feinberg R, et al. ACPA resource guide to chronic pain medication and treatment. American Chronic Pain Association. 2015. Available from http://www.theacpa.org/uploads/documents/ACPA_Resource_Guide_2015_Final%20edited%20%283%29.pdf. Accessed July 6, 2015.
3. Nuckols T, Anderson L, et. al. Opioid Prescribing: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain. Annals of Internal Medicine, Nov 12, 2013.
4. Chou R, Fanciullo G, et. al. Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. American Pain Society (APS). The Journal of Pain, Vol 10, No 2 (February), 2009: pp 113-130.
5. Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Published by the National Opioid Use Guideline Group (NOUGG). April 30 2010 Version 5.6 http://nationalpaincentre.mcmaster.ca/opioid/.
6. Guidelines for the Chronic Use of Opioids. American College of Occupational and Environmental Medicine (ACOEM). 2014.
7. Rolfs, R. Utah Department of Health (2009). Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain. Salt Lake City, UT: Utah Department of Health.
8. American Society of Interventional Pain Physicians (ASIPP) Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain: Part 2 – Guidance. Pain Physician 2012; 15:S67-S116.
9. VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. May, 2010.
10. Brennan MJ. Chronic pain: Overcoming treatment barriers for effective outcomes. Medscape. Available from http://www.medscape.org/viewarticle/495071. Accessed July 3, 2015.
11. Analgesic algorithm. World Health Organization. Last reviewed July 26, 2014. Available from https://www.icontrolmyhealth.org/disease/pain/management/analgesic-algorithm. Accessed Ju
12. Marcus DA. Treatment of nonmalignant chronic pain. Am Fam Physician. 2000; 61(5): 1331 – 1338. Available from http://www.aafp.org/afp/2000/0301/p1331.html. Accessed on July 2, 2015.
13. World Health Organization (WHO) ladder. World Health Organization. Available from http://www.geriatricpain.org/Content/Management/Interventions/Documents/WHO%20ladder.pdf. Accessed July 3, 2015.
14. Derry CJ, Derry S, Moore RA. Single dose oral ibuprofen plus paracetamol (acetaminophen) for acute postoperative pain (Review). The Cochrane Collaboration. 2013.
15. Teater, Donald. Evidence for the Efficacy of Pain Medications. National Safety Council. 2014.
16. Schug SA, Goddard C. Recent Advances in the pharmacological management of acute and chronic pain. Annals of Palliative Medicine 2014;3(4):263-275.

Neuropathic Pain Prescribing Algorithm



ATTENTION:

- Start at lowest dose and slowly taper up to maximum dose of one agent before adding or starting another drug.
- Depending on patient specifics, can maneuver within Line/Color Zones
- Intrathecal opioids are more effective than oral in patients unsuccessful on oral opioids.
- *Based on GI/Cardio Patient History
- ** Abuse Potential as a non-controlled substance
- *** Trigeminal Neuralgia only
- **** Watch for concominant CNS Depression

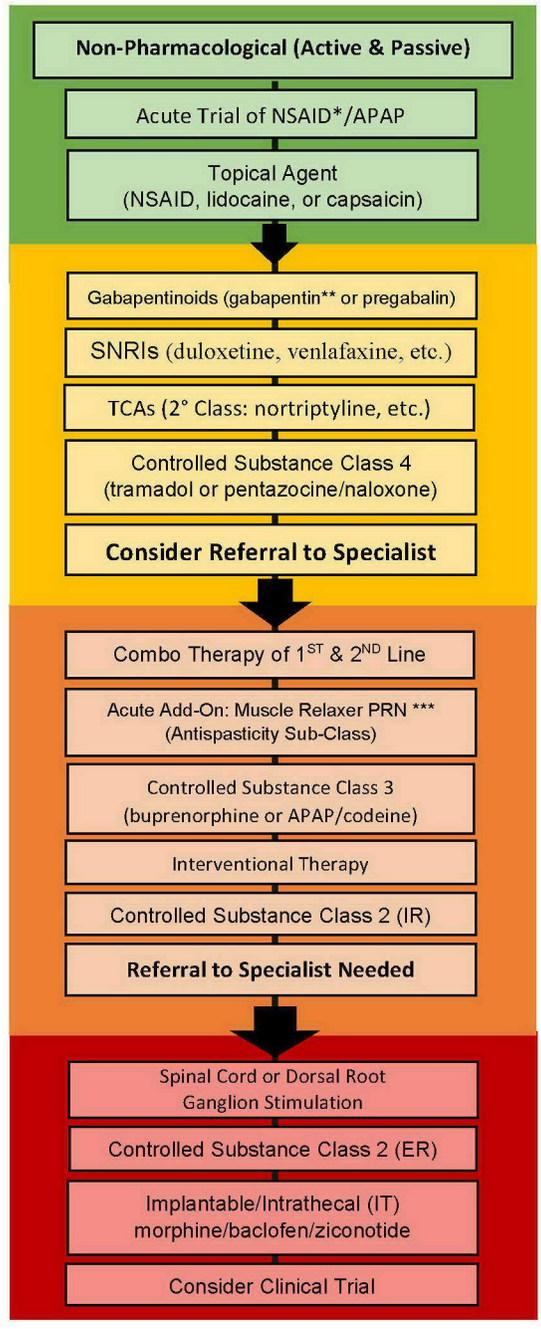
ABBREVIATIONS:

NSAID: Non-Steroidal Anti-Inflammatory Drug
APAP: acetaminophen
SNRI: Serotonin Norepinephrine Reuptake Inhibitor
TCA: Tricyclic Antidepressants
AEDs: Anti-Epileptic Drugs
CBZ: Carbemazepine
VPA: Valproic Acid
PRN: As Needed
IR: Immediate Release

References:

1. Hooten WM, Timming R, Belgrade M, et al. Assessment and Management of Chronic Pain. [6th Edition, 2013]. Institute for Clinical Systems Improvement (ICSI).
2. Christian J, Darnall B, Feinberg R, et al. ACPA resource guide to chronic pain medication and treatment. American Chronic Pain Association. January 2015.
3. Nuckols T, Anderson L, et. al. Opioid Prescribing: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain. Annals of Internal Medicine, Nov 12, 2013.
4. Chou R, Fanciullo G, et. al. Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. American Pain Society (APS). The Journal of Pain, Vol 10, No 2 (February), 2009: pp 113-130.
5. Finnerup, NB, Attal N, et. al. Pharmacotherapy for Neuropathic Pain in Adults: A Systematic Review and Meta-analysis. Lancet Neurol 2015; 162-173.
6. Neuropathic pain –pharmacological treatments. National Institute for Health and Care Excellence (NICE) Clinical Guideline 173. [Updated December 2014].
7. Schreiber AK, Nones CFM, et. al. Diabetic Neuropathic Pain: Physiopatho0logy and Treatment. World Journal of Diabetes. April 2015; 6(3): 432-444.
8. Moore RA, Chi CC, et. al. Oral Nonsteroidal Anti-inflammatory Drugs for Neuropathic Pain (A Cochrane Collaboration Review). 2015.
9. Ngian GS, Guymer EK, et. Al. The Use of Opioids in Fibromyalgia. International Journal of Rheumatic Diseases 2011; 14: 6-11.
10. Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Published by the National Opioid Use Guideline Group (NOUGG). April 30 2010 Version 5.6 http://nationalpaincentre.mcmaster.ca/opioid/.
11. Guidelines for the Chronic Use of Opioids. American College of Occupational and Environmental Medicine (ACOEM). 2014.
12. Rolfs, R. Utah Department of Health (2009). Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain. Salt Lake City, UT: Utah Department of Health.
13. American Society of Interventional Pain Physicians (ASIPP) Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain: Part 2 – Guidance. Pain Physician 2012; 15:S67-S116.
14. VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. May, 2010.
15. Schug SA, Goddard C. Recent Advances in the pharmacological management of acute and chronic pain. Annals of Palliative Medicine 2014;3(4):263-275.

Mixed Pain (Neuropathic & Nociceptive) Prescribing Algorithm



ATTENTION:

- Start at lowest dose and slowly taper up to maximum dose of one agent before adding or starting another drug.
- Depending on patient specifics, can maneuver within Line/Color Zones
- Intrathecal opioids are more effective than oral in patients unsuccessful on oral opioids.
- *Based on GI/Cardio Patient History
- **Abuse Potential as a non-controlled substance
- *** Watch for concominant CNS Depression

ABBREVIATIONS:

OTC: Over-the-Counter
APAP: Acetaminophen
NSAID: Non-Steroidal Anti Inflammatory Drug
ASA: Aspirin
IBU: Ibuprofen
SNRI: Serotonin Norepinephrine Reuptake Inhibitor
TCA: Trycyclic Antidepressant
IR: Immediate Release
PRN: As Needed

1. Hooten WM, Timming R, Belgrade M, et al. Assessment and Management of Chronic Pain. [updated November 2013]. Institute for Clinical Systems Improvement. Available at https://www.icsi.org/_asset/bw798b/ChronicPain.pdf. Accessed July 6, 2015.
2. Christian J, Darnall B, Feinberg R, et al. ACPA resource guide to chronic pain medication and treatment. American Chronic Pain Association. 2015. Available from http://www.theacpa.org/uploads/documents/ACPA_Resource_Guide_2015_Final%20edited%20%283%29.pdf. Accessed July 6, 2015.
3. Nuckols T, Anderson L, et. al. Opioid Prescribing: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain. Annals of Internal Medicine, Nov 12, 2013.
4. Chou R, Fanciullo G, et. al. Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. American Pain Society (APS). The Journal of Pain, Vol 10, No 2 (February), 2009: pp 113-130.
5. Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Published by the National Opioid Use Guideline Group (NOUGG). April 30 2010 Version 5.6 http://nationalpaincentre.mcmaster.ca/opioid/.
6. Guidelines for the Chronic Use of Opioids. American College of Occupational and Environmental Medicine (ACOEM). 2014.
7. Rolfs, R. Utah Department of Health (2009). Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain. Salt Lake City, UT: Utah Department of Health.
8. American Society of Interventional Pain Physicians (ASIPP) Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain: Part 2 – Guidance. Pain Physician 2012; 15:S67-S116.
9. VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. May, 2010.
10. Brennan MJ. Chronic pain: Overcoming treatment barriers for effective outcomes. Medscape. Available from http://www.medscape.org/viewarticle/495071. Accessed July 3, 2015.
11. Analgesic algorithm. World Health Organization. Last reviewed July 26, 2014. Available from https://www.icontrolmyhealth.org/disease/pain/management/analgesic-algorithm. Accessed Ju
12. Marcus DA. Treatment of nonmalignant chronic pain. Am Fam Physician. 2000; 61(5): 1331 – 1338. Available from http://www.aafp.org/afp/2000/0301/p1331.html. Accessed on July 2, 2015.
13. World Health Organization (WHO) ladder. World Health Organization. Available from http://www.geriatricpain.org/Content/Management/Interventions/Documents/WHO%20ladder.pdf. Accessed July 3, 2015.
14. Derry CJ, Derry S, Moore RA. Single dose oral ibuprofen plus paracetamol (acetaminophen) for acute postoperative pain (Review). The Cochrane Collaboration. 2013.
15. Teater, Donald. Evidence for the Efficacy of Pain Medications. National Safety Council. 2014.
16. Schug SA, Goddard C. Recent Advances in the pharmacological management of acute and chronic pain. Annals of Palliative Medicine 2014;3(4):263-275.

Non-Pharmacologic Treatment Options (Appendix 10.0)

Active & Passive Therapies

Pharmacological Treatment Options (Appendix 11.0)

Non-Opioids, Opioids, & Herbals and Supplements

Safe & Appropriate Opioid Use

(Suggestions in addition to clinical treatment algorithms and overall guidance)

1. Reduction in average Morphine Milligram Equivalents per day (MME/Day).
   - If continuing opioid use > 50 MME/Day, opioid tapering or pain management specialist referral is suggested.*
   - Established patients already on these relatively higher opioid daily doses should be offered the opportunity to reevaluate their pain management treatment plan in light of the association of opioid dosage and overdose risk.
2. Avoidance of combinations of opioids, benzodiazepines, muscle relaxers, and/or hypnotics due to severity of drug-drug interactions and increased chance for side effects. **
3. Preferred use of IR (immediate-release) compared to ER (extended-release) opioids, but when ER opioids are appropriate and selected, the abuse-deterrent formulations are preferred.
4. When a person does experience a non-life-ending overdose from a prescription opioid medication, the respective prescriber should be notified as soon as time permits, in order to follow-up with re-assessment of risk assessment and course of treatment, along with evaluation of possible substance use disorder.

In order to ensure safe and appropriate pain management, regulations have been passed in WV to update continuing education (CME, CPE, CE, etc.) requirements and also to define what a pain clinic is. Highlights of these regulations are included in Appendix 12.0 , with full text available online at www.legis.state.wv.us, as Senate Bill 437 of the year 2012.

*Evidence is insufficient to determine the effectiveness of long-term opioid therapy for reducing chronic pain and increasing daily function. Evidence supports a dose-dependent risk for serious harms (Chou R T. J., 2015).

**Overdose from benzodiazepines steadily rose from 1996 to 2010, parallel to the amount of benzodiazepines prescribed and dispensed (Appendix 13.1), similar to that parallel correlation of the amount of opioids sold compared to opioid overdoses in the same time frame (Appendix 13.2). Benzodiazepine overdose has plateaued since 2010, however, opioid overdoses have consistently still increased. (American Journal of Public Health, February 2016, Bachhuber et al., E1-E3) Appendix 13.0

CDC Opioid-Prescribing Guidelines (2016)

Determining when to initiate or continue opioids for chronic pain

1. Non-pharmacologic therapy and non-opioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with non-pharmacologic therapy and non-opioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients at least every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

*All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required). (CDC, 2016)

Healthcare Professional Responsibility of Safety

The most important concept within these pain management guidelines is the intent to assist in providing the highest level of appropriate, effective, and safe pain management for any and every patient. It is the responsibility of all healthcare professionals to collaborate at the highest level of care to not only "do no harm", but also appropriately, effectively, and safely take care of a patient's healthcare needs considering all available resources. These guidelines are based upon the best available evidence and clinical experience of the panel at the time of development. These guidelines intend to increase patient, prescriber, and dispenser safety and are not to be interpreted as a standard of care, but rather, as a resource to providers going forward as the treatment of chronic pain evolves away from chronic opioid use to other evidence based therapies.

Conclusion

One must agree that something, or better yet, some things need to change in order to address the psychological, moral, social, and healthcare concerns embedded within the cultural issue of substance use disorders and overdoses stemming from an overreliance on prescription pain medications within pain management. The work of this panel is intended to not only provide a risk reduction process, but ultimately to improve patient care and preserve human lives. By collaborating together and utilizing the steps within the proposed risk reduction process and the clinical pain treatment algorithms, healthcare professionals can best serve the needs of our residents to go beyond doing no harm, to provide appropriate, safe, and effective care. All healthcare professionals have a corresponding responsibility to not only ensure that any medication, controlled substances in particular, are being issued for a legitimate medical purpose by an individual practitioner acting in the usual course of his/her professional practice, but also to ensure appropriate patient care in general. Inherent within this concept, and this pain management guidance overall, is an effort of teamwork amongst healthcare professionals to seek additional professional opinions when appropriate, and ultimately ensure the highest level of patient care. Continued healthcare professional education can naturally allow said professionals to then educate the general population, and we, as a society, will then make large steps forward in addressing this impactful issue of epidemic proportion.

In summary, the preceding guidance on safe and effective pain management is intended to ultimately preserve our primary goal as healthcare professionals, of improving the quality of human life and saving lives.

Evidence Based References

(SAMHSA), S. A. (2006). *Treatment Improvement Protocol (TIP) Series, No 47.*

"Opioid Risk Assessment Tools". (2016, January 14). Retrieved from Opioid Risk: www.opioidrisk.com

Adams L, e. a. (2004). Development of a Self-Report Screening Instrument for Assessing Potential Opioid Medication Misuse in Chronic Pain Patients. *Journal of Pain and Symptom Management*, 440-460.

Administration, U. F. (2015, October). *Safe Medicine Disposal Options.* Retrieved from FDA: http://www.fda.gov/Drugs/NewsEvents/ucm464197.htm

Association, C. M. (2014). *Pain Management Guidelines.*

Brandeis University, C. o. (October 2014). *Mandating PDMP Participation by Medical Providers: Current Status and Experience in Selected States.* Retrieved from http://www.pdmpexcellence.org/sites/all/pdfs/COE_briefing_mandates_2nd_rev.pdf

Buprenorphine. (2006, November/December). *Palliativedrugs.com Newsletter*.

Butler S, e. a. (2007). Development and Validation of the Current Opioid Misuse Measure. *Pain*, 144-156.

CDC. (2016). *CDC Guideline for Prescribing Opioids for Chronic Pain - United States, 2016.* Morbidity and Mortality Weekly Report.

CDC Prevention for States. (2016, March 16). Retrieved from www.cdc.gov: http://www.cdc.gov/drugoverdose/states/state_prevention.html

Center, P. T. (2016, January 12). *Implementing Best Practices: A Comparison of PDMP Changes 2010 to 2014.* Retrieved from PDMP Assist: http://www.pdmpassist.org/pdf/state_survey_comparisons_TAG_FINAL_20151222.pdf

Chou R, e. a. (2009). Opioids for Chronic Non-Cancer Pain: Prediction and Identification of Aberrant Drug-Related Behaviors: A Review of the Evidence for an American Pain Society and American Academy of Pain Medicine Clinical Practice Guideline. *Journal of Pain*, 131-146.

Chou R, T. J. (2015, February 17). The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop. *Annals of Internal Medicine*, 276-96.

Clinical Pharmacology. Internet Database. (n.d.).

CMS. (2015, March). *Opioid EQ Conversion Factors*. Retrieved from www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-March-2015.pdf

Compton P, e. a. (2008). Introduction of a Self-Report Version of the Presciption Drug Use Questionnaire and Relationship to Medicaiton Agreement Noncompliance. *Journal of Pain and Symptom Management*, 383-396.

Cuschieri RJ, e. a. (1984). Comparison of Morphine and Sublingual Buprenorphine Following Abdominal Surgery. *Br. J. Anaesth.*, 855-859.

Danelich IM, e. a. (2015). *Pharmacotherapy, 10*, 1584.

Education, N. C. (2016, January 6). *Tips on Safe Storage and Disposal of Your Prescription Medicines.* Retrieved from http://www.talkaboutrx.org/documents/safe_storage.pdf

Fine P, P. R. (2009). Establishing "Best Practices" for Opioid Rotation: Conclusions of an Expert Panel. *Journal of Pain and Symptom Management*, 418-425.

Group, W. S. (May 2015). *Interagency Guideline on Prescribing Opioids for Pain.*

Harden P, A. S. (2015). Clinical Implications of Tapering Chronic Opioids in a Veteran Population. *Pain Medicine, 16*, 1975-1981.

Instructions for Healthcare Professionals: Prescribing Naloxone. (2016, January 12). Retrieved from Prescribe to Prevent: http://www.prescribetoprevent.org/wp-content/uploads/2012/11/one-pager_12.pdf

Jones CM, M. K. (2013). Pharmaceutical Overdose Deaths, United States, 2010. *JAMA, 309*, 657-659.

Khanna Ish, e. a. (2015). Buprenorphine - an attractive opioid with underutilized potential in treatment of chronic pain. *Journal of Pain Research*, 859-870.

Krebs EE, L. K. (2009). Development and Initial Validation of the PEG, a three-item scale assessing pain intensity and interfeerence. *J Gen Intern Med*, 733-738.

Lanser P, G. S. (2001). The 5th Vital Sign. *Pain Management, 8*, 68-70.

MMWR, C. (January 1, 2016, January 2016 1). *Morbidity and Mortality Weekly Report (MMWR).* Retrieved from http://www.cdc.gov/mmwr.

Olson, K. (2012). *HealthPartners Physician Leadership.* Retrieved from http://www.imehealthpartners.com/

Owen G, B. A. (2012). Urine Drug Testing: Current Recommendations and Best Practices. *Pain Physician*, ES119-ES133.

Pain Physician. (2010). *13*, 401-435.

Palliative Drugs. (n.d.). Retrieved from www.palliativedrugs.com

Paulozzi LJ, B. D. (2006). Increasing Deaths from Opioid Analgesics in the United States. *Pharmacoepidemiol Drug Safety, 15*, 618-627.

Paulozzi LJ, J. C. (2011). *Overdoses of Prescription Opioid Pain Relievers — United States, 1999–2008.* Morbidity and Mortality Weekly Report (MMWR). CDC.

Safeguard, D. (2011). *Counting Patient's Medication Protocol Sample.* Retrieved from http://www.doctorssafeguard.com/info/PAP/Pill%20Count%20Protocol%20-%20Example.pdf

SAMSHA. (2013). *National Survey on Drug Use and Health (NSDUH).* Retrieved from http://www.samhsa.gov/data/sites/default/files/NSDUH-SR200-RecoveryMonth- 2014/NSDUH-SR200-RecoveryMonth-2014.htm

Singh, B. &. (2008, June). Genetic Factors in Drug Metabolism. *American Family Physician, 77*(11), 1553-1560. Retrieved from Genetic Factors in Drug Metabolism: http://www.aafp.org/afp/2008/0601/p1553.html

Smith, H. (2009). Opioid Metabolism. *Mayo Clin Proc*, 613-624.

Smith, H. (2009). Opioid Metabolism. *Mayo Clin Proc*, 613-624.

Tolia, V. (2015). Increasing Incidence of the Neonatal Abstinence Syndrome in U.S. Neonatal ICUs. *The New England Journal of Medicine*, 2118-2126.

Trippe B, e. a. (2016). Nutritional Management of Patients with Diabetic Peripheral Neuropathy with L-methylfolate-methylcobalamin-pyridoxal-5-phosphate: Results of a Real-World Patient Experience Trial. *Current Medical Research & Opinion*, 219-227.

USDTL. (2016). Retrieved from United States Drug Testing Laboratories, Inc.: http://www.usdtl.com/testing/meconium-drug-test-labs

Webster, L. (2012). What are best safety practices for use of methadone in the treatment of pain? *Practical Pain Management*.

Webster, L. (2013). The Role of Urine Drug Testing in Chronic Pain Management: 2013 Update. *Pain Medicine News*, 45-50.